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EXAMINER	
WHITEMAN, BRIAN A	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 01/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/672,407	MORALES-LEVY ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply w. Seq.*.

DETAILED ACTION

Non-Final Rejection

Claims 1-10 are pending.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 or 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 10/313,463 or 60/340,141, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

The genus of nucleic acids in the instant claims are not supported under 112 first paragraph written description in parent application '463 or '141. Neither '463 nor '141 disclose using an immunostimulatory sequence (which does not comprise an antigen which a protective immune response is desired) or the nucleic acid is a phosphorothioate analogue in the method for inhibiting fertility in a female mammal. Both applications

provide written description for a nucleic acid encoding a ZP peptide in the method of inhibiting fertility in a female mammal. Thus, the claimed genus of nucleic acids only has benefit to the filing date of the instant application.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See page 7. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The disclosure is objected to because of the following informalities: catalog nos. on page 20 are missing.

Appropriate correction is required.

This application contains sequence disclosures that are encompassed by the definition for nucleotide sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements for Patent Applications Containing Nucleotide Sequence Disclosures.

The sequences on pages 17, 18, 27, and 31-33 are missing a corresponding SEQ ID NO:.

A complete response to the instant office action should include a response to the Notice to Comply Letter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-10, as best understood, are readable on a genus of nucleic acids that inhibit fertility in a female mammal, wherein the genus of the nucleic acids is not claimed in a specific biochemical or molecule structure that could be envisioned by one skilled in the art at the time the invention was made.

The claimed genus embraces nucleic acids that are phosphorothioate analogues, oligonucleotides, immunostimulatory sequences (ISS). The specification discloses a nucleic acid encoding a ZP peptide that can be used to inhibit fertility of a female mammal (pages 11-12). The specification further discloses ISS sequences built around a central CpG dinucleotide sequences (page 12). The species of nucleic acids within the claimed genus varies. The disclosure provides sufficient description for the nucleotide sequences disclosed on page 27 and a nucleic acid encoding ZP peptide or an oligonucleotide comprising a CpG dinucleotide sequences. However, the prior art teaches that CpG are used to enhance fertility in a mammal not inhibit fertility in a mammal (See US 20030109531). The specification does not provide sufficient

description of a genus of nucleic acids. It is not apparent that on the basis of the applicants' disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the claimed invention and reference to potential methods and/or molecular structures of molecules that are essential for the genus of nucleic acids that must exhibit the disclosed biological functions as contemplated by the specification.

It is not sufficient to contemplate the claimed genus of nucleic acids to sufficiently support the present claimed invention directed to a genus of nucleic acids that inhibit fertility in a female mammal. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and which is not conventional in the art as of applicant's effective filing date. Claiming a genus of nucleic acids, that must possess the biological properties as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of a nucleic acids that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless

of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibiting fertility in female mice comprising administering a nucleic acid as specifically set forth on page 27, lines 10-13 and for inhibiting fertility in female Balb/c mice comprising administering a nucleic acid encoding a zona pellucida peptide as set forth in SEQ ID NO: 1, does not reasonably provide enablement for inhibiting fertility in a female mammal using a genus of nucleic acid that inhibit fertility. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims read on using a genus of nucleic acids for *in vivo* administration to a genus of female mammals to inhibit fertility in the mammals. The nucleic acid could encode a peptide, an oligonucleotide, an ISS or a phosphorothioate analogue. Thus, the claims are considered broad. The claims will therefore be evaluated based upon *in vivo* use of a nucleic acid.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (United States v. Telectronics, Inc., 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is required is not based

upon a single factor, but rather a conclusion reached by many factors. These factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in In Re Wands (see above).

The prior art exemplified by Anderson et al., *Nature*, Vol. 392, pp. 25-30, 1998, displays major consideration for any nucleic acid therapy protocol involve issues that include:

1) The type of vector and amount of DNA constructs to be administered,

2) The route and time course of administration, the sites of administration, and successful uptake of the claimed DNA at the target site;

3) The trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA product, the amount and stability of the protein produced, and

4) What amount of the expressed proteins considered to be therapeutically effective for a DNA therapy method.

In addition, all of these issues differ dramatically based on the specific vector used, the route of administration, the mammal being treated, and therapeutically effective amount of the DNA.

Anderson teaches that nucleic acid therapy is a powerful new technology that still requires several years before it will make a noticeable impact on the treatment of disease, and that several major deficiencies still exist including poor delivery systems, both viral and non-viral, and poor gene expression after nucleic acids are delivered (pp. 25-30).

Anderson further teaches that the reason for the low efficiency of nucleic acid transfer and expression in human patients is that we still lack the basis understanding of

how vectors should be constructed what regulatory sequences are appropriated for which cell types (page 30, column 1, last paragraph). Furthermore, Verma, *Nature*, Vol. 389, pages 239-242, 1997, indicates that factors including the nature of a DNA and/or target tissue and a delivery system and/or amounts of the DNA complexes employed in the delivery system that would generate a therapeutic effect *in vivo* must be considered for any nucleic acid therapy method to be successful (page 238, columns 1 and 2). For additional reviews of the unpredictability of nucleic acid therapy (e.g., DNA vaccines) or contraceptive vaccines, see Aitken, Journal of Reproductive Immunology, 57: 273-287, 2002; Frayne et al., Journal of Reproductive Immunology, 43:1-33, 1999; McLaughlin et al. Expert Opin. Biol. Ther., 3:829-841, 2003; Lou et al. The Journal of Immunology, 1995, 155:2715-2720; McCluskie et al. Molecular Medicine, 5, pp. 287-300, 1999; Paterson et al. Journal of Reproductive Immunology, 53: 99-107, 2002. Therefore, at the time the application was filed, nucleic acid therapy was considered unpredictable.

Applicants teach an immunization protocol where a plasmid comprising a nucleic acid encoding PZP-3a (SEQ ID NO: 1) or a control was either intradermally (ID) administered at the base of the tail or intramuscularly (IM) delivered into hindquarters of female Balb/C mice. Then, the mice were caged together with male mice for 6 consecutive days. Table 2 in the instant specification displays that 1/5 female mice given the plasmid ID were pregnant and 2/5 female mice that were given the plasmid IM were pregnant. In the control group, 2/5 female mice given the control plasmid were pregnant. Applicants further teach administering ISS having a specific sequence to female mice produce transient contraception.

At the time of filing, the prior art for using a nucleic acid encoding a zona pellucida peptide for inhibiting fertility in several different species of female mammals was well known to the skilled artisan. However, the prior art teaches that, "the feasibility of a ZP3 contraceptive vaccine has been marred by the finding that ZP3-specific T cells mediate ovarian autoimmune disease. Moreover, as reported in this work, only some inbred mouse strains respond to the ZP3 peptide" (Lou, supra). In view of the art of record, the results from the examples in the specification would not lead one skilled in the art to use a genus of nucleic acids to inhibit fertility in a genus of female mammals. The focus of the examination inquiry is whether everything within the scope of the claim is enabled. See MPEP 2164.08.

Furthermore, with respect to extrapolation from the mouse model taught in the specification to inhibiting fertility in a genus of female mammals (e.g., non-human primate, human, cat, dog, deer, cow, rabbit, squirrel, fox, etc.) set forth in the claimed invention, the state of art exemplified by McCluskie et al. (supra) teach that "the realization that results in mice often do not predict the situation in humans has also led to a large number of DNA vaccine studies in non-human primates, that IM injection of plasmid DNA vaccines, while highly immunogenic in mice...was found only to be relatively so in chimpanzees..., and especially not all in Aotus monkeys" and that "it is probably safe to say that any vaccine that works in a human will work in a mouse, but not necessarily vice-versa" (page 296, column 2, second and third paragraphs). In addition, McCluskie et al. teach that "although non-human primate models are frequently used for development and testing of human vaccines, it is not clear how predicative they will be in the case of DNA vaccines where efficacy, by virtue of the requirement first to transfect

cells and express the antigen, relies on many factors other than immunological responses to the antigen" (page 297, column 1).

Thus, it is not apparent as to how one skilled in the art reasonably extrapolates, without undue experimentation, from the disclosures in the specification as filed to the claimed invention that would generate inhibition of fertility (reversible/irreversible) in a genus of mammals. Even if an inhibition response has been shown in female mice using the exemplified Balb/c female mice, it is not apparent as to how the female mouse model is reasonably extrapolated to the full scope of the claimed invention encompassing a genus of female mammals; particularly given that there is no vaccine generation evidence showing that the mouse model is a general phenomenon, and given the doubts expressed in the art of record.

Furthermore, the claims read on either inhibiting fertility by inhibiting sperm-egg binding, which can be reversible or ovarian pathology (this is characterized by a premature loss of ovarian function associated with the demise of the primordial follicle pool, a situation from which the ovary cannot overcome (Paterson, supra). In addition to the reasons set forth above for the invention not being enabled, the applicants do not teach if sperm-egg binding was inhibited or ovarian pathology was observed in the female mice. The prior art teaches that adverse autoimmune reactions have been observed in mice following induction of immunity to mouse ZP3 (Paterson, supra).

Furthermore, applicants teach an ELISA isotyping assay in female injected with ZP-NAV (see table 3) and standard ZP vaccine and antibody titers for females injected once with ZP-NAV (see table 4). However, the relevance of this data to inhibiting fertility *in vivo* is unclear at best because neither the applicants nor the prior art provide a

correlation or nexus between the results obtained in *in vivo* studies such as those provided by applicants so that the skilled artisan can practice the claimed method without an undue amount of experimentation.

As a result, it is not apparent how one skilled in the art determines, without undue experimentation, which of the claimed nucleic acids, how is it apparent as to how one skilled in the art, without any undue experimentation, practices any nucleic acid therapy method as contemplated by the claims, particularly given the unpredictability of nucleic acid therapy as a whole and/or the doubts expressed in the art of record.

Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be concluded that the skilled artisan would have need to have concluded undue experimentation in order to practice the claimed invention.

Furthermore, with respect to using a genus of nucleic acids in the claimed invention, the specification fails to provide adequate guidance for making a nucleic acid to inhibit fertility in a female mammal. The broadest claims read on a nucleic acid inhibiting fertility. The prior art teaches that CpG are used to enhance fertility in a mammal not inhibit fertility in a mammal (See US 20030109531). The as-filed specification does not provide sufficient guidance and/or factual evidence for one skilled in the art to make and/or use a nucleic acid other than the nucleic acid specifically disclosed on page 27 and a nucleic acid encoding a ZP peptide. The claimed invention also embraces nucleic acid encoding a ZP peptide from ZPA, ZPB, ZPC and that is either glycosylated or deglycosylated. The specification recites: "a zona pellucida peptide refers to an egg specific protein or portion thereof of the mammalian oocyte involved in

the binding with sperm and the induction of the acrosome reaction which is essential for the penetration and subsequence fertilization of the egg" (page 4). The specification provides no guidance as to which (if any) of the amino acids encoded by the nucleic acid of ZP peptide may be changed while the claimed biological activity (e.g., inhibit sperm-egg binding or loss of ovarian function associated with the demise of the primordial follicle pool) is retained. The effects of these changes is largely unpredictable as to which ones have a significant effect versus not. Several publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over polypeptides of related function upon a significant amount of further research. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain fertility inhibition, and the fact that the relationship of the sequence of a peptide and its tertiary structure (*e.g.* its activity) are not well understood and are not predictable (Ngo et al. The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495), it would require an undue amount of experimentation for one skilled in the art in view of the prior art to arrive at other nucleic acids that possess the claimed biological activity. Since it would require undue experimentation to identify other peptides that inhibit fertility in a female mammal, it certainly would require undue experimentation to make their corresponding DNA, and therefore, the entire scope of the claimed invention.

In conclusion, the as-filed specification and claims coupled with the prior art at the time the invention was made do not provide sufficient guidance and/or evidence to reasonably enable the full scope claimed invention. Given that DNA vaccines wherein

any nucleic acid is employed to inhibit fertility in a female mammal was unpredictable at the time the invention was made, and given the lack of sufficient guidance as to a DNA vaccine effect produced by any nucleic acid cited in the claims, one skilled in the art would have to engage in a large quantity of undue experimentation in order to practice the claimed invention based on the applicants' disclosure and the unpredictability of DNA vaccines.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
> (f) he did not himself invent the subject matter sought to be patented.

Claims 1-4 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Kerr et al. (Biology of Reproduction, 61, 606-613, 1999). Kerr teaches a method of inhibiting fertility in female rabbits with rabbit zona pellucida protein ZPB as expressed by recombinant myxoma virus (page 606). Kerr teaches the limitation in claim 7 (page 607).

Claims 1-4 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by de Jersey (Reprod. Fertil. Dev. 1999, 11, 219-228). de Jersey teaches a method of inhibiting

fertility in female foxes using a Salmonella typhimurium expressing bacterial and sperm proteins (page 219). de Jersey teaches the limitation in instant claim 8 (page 221).

Claims 1-4 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Curtiss et al. (US 5656488). Curtiss teaches a method of inhibiting fertility in a female mammal comprising administering an avirulent microbe derived from a pathogenic gram negative microorganism selected from the group consisting of Salmonella, Escherichia, and Salmonella-Escherichia hybrids comprising a recombinant expression system which encodes at least one gamete-specific antigen that is displayed on the surface of gametes exposed during the process leading to fertilization, wherein the avirulent microbe, upon administration to an individual, is capable of colonizing a lymphoreticular tissue and eliciting a mucosal immune response (columns 51-54). Curtiss teaches the limitation in instant claim 8 (column 15).

Claims 1, 2, 3, 4, and 9 are rejected under 35 U.S.C. 102(e) as being anticipated by Metelev et al. (US 6831676). Metelev teaches using a hybrid oligonucleotide phosphorothioates, wherein the oligonucleotide comprises a sequence that inhibits the expression of a protein in a female that is necessary for fertility (column 16).

Claims 1-3 and 6 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. The claims in US Application No. 10/313,463 are directed to a method of inhibiting fertility in a female mammal comprising administering a nucleic acid encoding a peptide.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 6-8, and 10 are rejected under 35 U.S.C. 103(a) as being obvious over Morales-Levy et al. (US 20030181409, US application 10/313,463).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Morales-Levy teaches a method of inhibiting fertility in a female mammals comprising administering a nucleic acid encoding a ZP3 peptide comprising SEQ ID NO; 3. Morales-Levy teaches the limitation in claim 6 (claim 5). Morales-Levy teaches the limitation in claims 7, 8 and 10 (page 12).

Claims 1 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kerr et al. (Biology of Reproduction, 61, 606-613, 1999) taken with Curtiss et al. (US 6383496). Kerr teaches a method of inhibiting fertility in female rabbits with rabbit zona

pellucida protein ZPB as expressed by recombinant myxoma virus (page 606). However, Kerr does not specifically teach oral administration of the virus.

However, at the time the invention was made, oral administration of a recombinant virus was well known to one of ordinary skill in the art as exemplified by Curtiss et al. (column 18).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Kerr take with Curtiss, namely to oral administration the recombinant virus. One of ordinary skill in the art would have been motivated to combine the teachings because oral administration is non-stressful, requires little labor, and can be applied at a large scale.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Curtiss et al. (US 5656488). However, Curtiss does not specifically teach the limitation recited in instant claim 10.

With respect to the limitation directed to dosage used to induce infertility used in the claimed method.

MPEP 2144.05 recites: Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine

experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). This is the case here. The specification (page 14) does not disclose that the limitation in instant claim 10 is critical for one of ordinary skill in the art to practice the claimed invention.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made, namely to administration the recombinant virus at a dose between about 50ug/kg and about 1mg/kg. One of ordinary skill in the art would have been motivated to use a dose about 50ug/kg and about 1mg/kg because Curtiss teaches that the dosages of the compositions comprising ZP which can prevent or reduce fertility can be determined in view of this disclosure by one of ordinary skill in the art by running routine trials with appropriate controls.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a

nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 6-8, and 10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2, 4, 5, 6, 7 and 9-10 of copending Application No. 10/313,463. Although the conflicting claims are not identical, they are not patentably distinct from each other because both set of claims are directed to inhibiting fertility in a female mammal comprising administering a nucleic acid encoding a peptide.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-3, 6-8, and 10 are directed to an invention not patentably distinct from claims 2, 4, 5, 6, 7, 9, and 10 of commonly assigned US patent application 10/313,463. Specifically, for the reasons set forth under the provisional double patenting rejection.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned US application, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR

1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US 20040198671 could be used in a 102(e) rejection over claims 1-4 but the claims are already rejected under 102(e).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, acting SPE – Art Unit 1635, can be reached at (571) 272-0811.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the

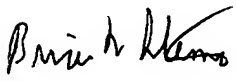
Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Brian Whiteman
Patent Examiner, Group 1635



Notice to Comply	Application No. 10/672,407	Applicant(s) Morales-Levy et al.	
	Examiner B. Whiteman	Art Unit 1635	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: The sequences on pages 17, 18, 27, and 31-33 are missing a corresponding SEQ ID NO: and there is not CRF.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the specification.**

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

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